

## WHAT IS CLAIMED IS:

1. A synthetic polynucleotide comprising a sequence encoding a human papillomavirus (HPV) protein, or mutated form of a HPV protein which has reduced protein function as compared to wild-type protein, but which maintains immunogenicity, the polynucleotide sequence comprising codons optimized for expression in a human host.
2. A polynucleotide according to Claim 1 wherein the protein is selected from the group consisting of: L1, L2, E1, E2, E4, E5, E6 and E7.
3. A polynucleotide according to Claim 2 wherein the protein is selected from the group consisting of: L1, E1, E2, and E7.
4. A polynucleotide according to Claim 2 which is DNA.
5. A polynucleotide according to Claim 4 wherein the protein is L1 and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, and HPV68.
6. A polynucleotide according to Claim 5 wherein the protein is an HPV16 L1 protein.
7. A polynucleotide according to Claim 6 which comprises the polynucleotide of FIGURE 1 (SEQ.ID.NO: 1).
8. A polynucleotide according to Claim 4 wherein the protein is an E1 protein or a mutated E1 protein and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, and HPV 68.
9. A polynucleotide according to Claim 8 wherein the protein is a mutated form of E1.

10. A polynucleotide according to Claim 8 which is an HPV16 E1 protein.
- 5 11. A polynucleotide according to Claim 10 which comprises the polynucleotide of FIGURE 2 (SEQ. ID.NO:2).
- 10 12. A polynucleotide according to Claim 4 wherein the protein is E2 protein or a mutated E2 protein and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, and HPV 68.
- 15 13. A polynucleotide according to Claim 12 wherein the protein is a mutated E2 protein.
14. A polynucleotide according to Claim 11 which is an HPV16 E2 mutated protein.
- 20 15. A polynucleotide according to Claim 14 which comprises the polynucleotide of FIGURE 3 (SEQ. ID.NO: 3).
- 25 16. A polynucleotide according to Claim 4 wherein the protein is E7 or an E7 mutant and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV68.
17. A polynucleotide according to Claim 16 wherein the protein is an HPV6a protein.
- 30 18. A polynucleotide according to Claim 17 which comprises the polynucleotide of FIGURE 4 (SEQ. ID.NO:4).

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19. An adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:
- 5 A) a polynucleotide encoding an HPV protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein the polynucleotide is codon-optimized for expression in a human host cell; and
- B) a promoter operably linked to the polynucleotide.
20. A vector according to Claim 19 wherein the adenoviral genome
- 10 also contains a deleted E3 region.
21. A shuttle plasmid vector comprising a plasmid portion and an adenoviral portion, the adenoviral portion comprising: an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises
- 15 an expression cassette comprising:
- A) a polynucleotide encoding an HPV protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein the polynucleotide is codon-optimized for expression in a human host cell; and
- B) a promoter operably linked to the polynucleotide.
- 20 22. A vaccine plasmid comprising a plasmid portion and an expression cassette portion, the expression cassette portion comprising:
- A) a polynucleotide encoding an HPV protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein the polynucleotide is codon-
- 25 optimized for expression in a human host cell; and
- B) a promoter operably linked to the polynucleotide.
23. A plasmid according to Claim 22 wherein the plasmid portion
- 30 is VIJs.
24. A method for inducing immune responses in a vertebrate which comprises introducing between 1 ng and 100 mg of the polynucleotide of Claim 1 into the tissue of the vertebrate.

25. A method for inducing immune responses in a vertebrate which comprises introducing between  $10^{11}$ - $10^{12}$  particles of an adenoviral vector carrying the polynucleotide of Claim 1 into the tissue of the vertebrate.

5 26. A method for inducing an immune response against human papillomavirus in a vertebrate, comprising

- A) introducing into the vertebrate a first vector comprising a polynucleotide encoding an HPV protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein the polynucleotide is codon-optimized for  
 10 expression in a human host cell;
- B) allowing a predetermined amount of time to pass; and
- C) introducing into the vertebrate a second vector comprising adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression  
 15 cassette comprises
- i) a polynucleotide encoding an HPV protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein the polynucleotide is codon-optimized for expression in a human host cell; and
- ii) a promoter operably linked to the polynucleotide.

20 27. A method according to Claim 26 wherein the vertebrate is human.

25 28. A method for inducing immune responses in a vertebrate comprising

- A) introducing into the vertebrate a plasmid vaccine, wherein the plasmid vaccine comprises a plasmid portion and an expression cassette portion, the expression cassette portion comprising:
- i) a polynucleotide encoding an HPV protein selected from the  
 30 group consisting of L1, E1, E2, and E7 proteins, wherein the polynucleotide is codon-optimized for expression in a human host cell; and
- ii) a promoter operably linked to the polynucleotide;
- B) allowing a predetermined amount of time to pass; and

C) introducing into the vertebrate an adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

- 5 i) a polynucleotide encoding an HPV protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein the polynucleotide is codon-optimized for expression in a human host cell; and
- ii) a promoter operably linked to the polynucleotide.

29. A method according to Claim 28 wherein the vertebrate is  
10 human.

30. A method of making a HPV protein comprising expressing in a host cell a synthetic polynucleotide encoding a human papillomavirus (HPV) protein, or mutated form of a HPV protein which has reduced protein function as compared to  
15 wild-type protein, but which maintains immunogenicity, polynucleotide sequence comprising codons optimized for expression in a human host.